we see no stability effect, we would say there is no significant change, no significant effect. But in this one we use slightly different language here. There is no adverse effect, which isn't going as far as to say there is a positive effect.

BY MR. GIBBONS:

Q Dr. Long, was Glaxo being conservative in its assertions of shelf-life in 1986?

A We were naturally conservative. Until we had a fuller picture of the data we were being conservative. At this time we had only had 6 months' data on the formulation containing ethanol. So it was a strong suggestion the ethanol was enhancing stability. Strong enough to be a near certainty but not strong enough to overcome our natural conservativeness when putting together an NDA submission.

Q Is it correct, Dr. Long, that the data, stability data, that was collected and assessed under your direction indicated that the addition of alcohol enhanced the stability of aqueous ranitidine syrup formulation?

A Yes, it was, and that was a very surprising finding.

Q Is that discovery accurately reflected in the April to October 1986 event on the trial exhibit 116, which is the '249 patent time line?

A Yes, that's correct.

Q Dr. Long, was a patent eventually filed by Glaxo with

Q Dr. Long, in your experience at Glaxo did you ever consider using propylene glycol as a preservative?
A Yes, we did.
Q Did it work as a preservative?
A It did not work at the, in the experiment we performed. What we did was to test Zantac Syrup containing propylene glycol, test against the organism *Pseudomonas cepacia*, and it was unsuccessful in dealing with that organism. But the concentration we used was set by the upper limit that we believed to be acceptable according to recommendations from the World Health Organization for propylene, or propylene glycol. There is a maximum recommended for that material. We used that in conjunction with the volume to be given on a daily basis to a subject in conjunction with the weight of the subject, in this case a 20-kilo subject, being a child, because again we were developing a product potentially for use in children. With all that information we set ourselves a level of 2.5 percent weight and volume and that was inserted to do with the problem of *Pseudomonas cepacia*.
Q I would like to direct your attention in plaintiffs' trial exhibit 238, specifically to pages Y084325 and 84326, and if you would look at 326 to the conclusion section, which states, quote, the addition of propylene glycol to Zantac Syrup does not enhance the preserving power of the system, close quote. That is the work date you were referring to?

A That's the work and it's got the year, the qualifier, 2.5 percent, in that conclusion.

Q I would like to turn your attention back again to Defendants' Exhibit 20, which is the file history of the '249 patent.

(Pause for document examination.)

Q Dr. Long, reviewing Claim 1 of the application as filed, which you testified to earlier, does that claim state that the use of ethanol is to kill microbial contamination?

A No, it doesn't, and that is not the basis of the patent.

Q But didn't you indeed add ethanol to the formulation to kill *Pseudomonas cepacia*?

A Yes, that was the reason for adding ethanol, but it was subsequently with the generation of stability data, the surprising enhancement of stability became known.

Q In any of the documents in Defendants' Exhibit 20 or Exhibit 19, which is the actual '249 patent, do you see anywhere in there where you told the Patent Office that the reason that you added ethanol was to kill *Pseudomonas cepacia*?

A The answer is no, because I know those words don't occur in the patent, *Pseudomonas cepacia*, and we would not have seen any reason to have put those words in because that's not the basis of the patent.